REMARKS/ARGUMENTS

Claims 58-62 are pending in this application.

Applicants note and appreciate the withdrawal of the earlier objections and rejections under 35 U.S.C. §101 and 35 U.S.C. §112, second paragraph. The remaining rejections under 35 U.S.C. §102 and 35 U.S.C. §103 are addressed below.

I. Information Disclosure Statement

Applicants thank the Examiner for considering the information disclosure statement submitted on September 9, 2005.

II. Claim Rejections Under 35 USC §102

Claim 58 remains rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Struyk *et al.* (The Journal of Neuroscience, 15(3):2141-2156, March 1995). Struyk *et al.* teach an isolated polypeptide having 91% amino acid sequence identity with SEQ ID NO:523, and a polyclonal antibody that binds to this polypeptide.

Applicants respectfully point out that, as discussed in the Response filed September 9, 2005, Claim 58 recites "an isolated antibody that specifically binds to the polypeptide of SEQ ID NO:523." (Emphasis added). Applicants respectfully submit that the term "specific binding" recited in Claim 58 refers to an antibody that binds to a particular epitope without binding to another epitope. Therefore, Claim 58 and the claims dependent from Claim 58, carrying its recitations, clearly refer to an antibody that is able to bind to a specific epitope of the PRO337 polypeptide of SEQ ID NO:523 *without* cross reacting with other epitopes, including those found in the sequence disclosed in Struyk *et al.* In view of this, the Examiner errs in assuming that the antibodies claimed in the present application would display significant binding to the polypeptide of Struyk *et al.*, and thus overlap with the antibodies disclosed in Struyk *et al.* As a result of the requirement of specific binding, the claims pending in this application do not encompass antibodies that specifically bind to epitopes found in the polypeptide of Struyk *et al.*

Clearly there exist specific epitopes in the SEQ ID NO:523 protein that are not found in the Struyk protein. One of ordinary skill in the art would readily understand that given the substantial divergence in sequence between the amino terminal regions of SEQ ID NO:523 and the polypeptide of Struyk *et al.* (as shown in Exhibit A of the Office Action mailed June 15,

2005), antibodies raised, for example, to the amino terminal region of SEQ ID NO:523 would specifically bind to SEQ ID NO:523, and would not bind to the polypeptide of Struyk *et al.*

One of ordinary skill in the art would further understand how to make and use such antibodies. The specification provides methods to determine whether an antibody specifically binds to epitopes possessed by SEQ ID NO:523. Routine methods of determining antibody binding specificities, including immunoprecipitation, or competitive binding assays such as radioimmunoassay (RIA) or enzyme-linked immunoabsorbent assay (ELISA), are disclosed in the specification at, for example, page 218, lines 17-20. Methods of determining the binding affinities of antibodies using Scatchard analysis are disclosed at page 218, lines 20-21. In addition, a method of using competitive binding assays to determine if a peptide shares an antigenic determinant for a particular antibody with a PRO polypeptide is disclosed in the specification at page 325, lines 25-28.

The Examiner asserts that "the claims do not require any particular epitope specificity of the claimed antibodies and the two polypeptides share many epitopes that are identical" and concludes that "the antibodies taught by Struyk *et al.* possess the same structural and functional properties as those of the antibodies claimed, i.e., specifically binds the polypeptide of SEQ ID NO:523." (Page 4 of the instant Office Action).

Applicants respectfully point out that the claims do not recite antibodies which specifically bind to an epitope. Rather, the claims recite antibodies that specifically bind to SEQ ID NO:523. That is, the recited antibodies recognize not merely specific epitopes, but epitopes which are specific to SEQ ID NO:523 and not, for example, to the protein of Struyk *et al.* Thus the issue to consider is not whether the antibodies of Struyk *et al.* bind to specific epitopes (as most antibodies do), but whether they bind to specific epitopes of SEQ ID NO:523, as would be demonstrated, for example, by a failure of the Struyk protein to significantly compete with SEQ ID NO:523 for binding to the Struyk antibody.

The reference antibodies of Struyk *et al.* do not anticipate the claims because these antibodies were raised to the Struyk protein and therefore would not be expected to have stronger binding to SEQ ID NO:523 than the Struyk protein. Applicants submit that indeed there may be antibodies that are capable of binding to epitopes present in both the PRO337 polypeptide and the Struyk protein. However, the present invention does not claim such antibodies.

Applicants note while related proteins may have a conserved tertiary structure, the additional factor of primary sequence diversity means that even structurally very similar proteins can still have unique epitopes. For example, it is well know that pathogenic viruses evade the host immune system by rapidly mutating sites on their structural proteins so that these proteins, while retaining the three-dimensional structure required for their proper function, are no longer recognizable by any of the antibodies generated to earlier viral strains. Furthermore, given the substantial divergence in sequence between the amino terminal regions of SEQ ID NO:523 and the polypeptide of Struyk *et al.* (as shown in Exhibit A of the Office Action mailed June 15, 2005), it would be clear to one of ordinary skill in the art that antibodies raised, for example, to the amino terminal region of SEQ ID NO:523 would specifically bind to SEQ ID NO:523 and would not bind to the polypeptide of Struyk *et al.*

The Examiner asserts that "applicant argues with limitations not recited in the rejected claim." Applicants respectfully point out that Claim 58 recites antibodies that specifically bind to SEQ ID NO:523. As discussed above, the term "specifically binds" in this context refers to antibody that is able to bind to a specific epitope of the PRO337 polypeptide of SEQ ID NO:523 *without* cross reacting with other epitopes, including those found in the sequence disclosed in Struyk *et al.* One of ordinary skill in the art, in making antibodies that specifically bind to SEQ ID NO:523, would therefore look for epitopes that are specific to SEQ ID NO:523, and would have as a logical consequence been led to the amino terminal region of SEQ ID NO:523.

The Examiner further asserts that "the amino terminal 28 amino acids are part of the signal peptide, which is cleaved from the protein during processing." (Page 5 of the instant Office Action). Applicants respectfully point out that Claim 58 recites antibodies that specifically bind to SEQ ID NO:523. The recited antibodies are not limited to binding only the cleaved form of SEQ ID NO:523, lacking its signal peptide. Antibodies that bind to the signal peptide region of SEQ ID NO:523 would be useful, for example, in purifying recombinant PRO337 produced in bacteria.

Accordingly, Struyk *et al.* does not anticipate the claimed antibodies that specifically bind to SEQ ID NO:523, and withdrawal of the rejection of Claim 58 under 35 U.S.C. §102(b) as anticipated by Struyk *et al.* is therefore respectfully requested.

III. Claim Rejections Under 35 USC §103

Claims 58-62 remain rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Struyk *et al.* in view of De Boer (U.S. Patent No. 5,874,082, filed February 23, 1996). Struyk *et al.* teach an isolated polypeptide having 91% amino acid sequence identity with SEQ ID NO:523, and a polyclonal antibody to this polypeptide. De Boer teaches monoclonal antibodies, humanized antibodies, antibody fragments, and labeled antibodies.

As discussed above, Struyk *et al.* does not disclose each and every limitation of Claims 58, or those claims dependent upon Claim 58, because Struyk *et al.* does not disclose antibodies that specifically bind to SEQ ID NO:523. De Boer does not cure the deficiencies of Struyk *et al.*, as De Boer teaches only general forms of antibodies, but does not disclose antibodies that specifically bind to SEQ ID NO:523. Thus Applicants respectfully submit that the instant claims are not obvious over Struyk *et al.* in view of De Boer.

Accordingly, withdrawal of the rejection of Claims 58-62 under 35 U.S.C. §103(a) over Struyk *et al.* in view of De Boer is respectfully requested.

CONCLUSION

In conclusion, the present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited. Should there be any further issues outstanding, the Examiner is invited to contact the undersigned attorney at the telephone number shown below.

Please charge any additional fees, including fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641** (referencing Attorney's Docket No. **39780-2630 P1C13**).

Respectfully submitted,

Date: December 16, 2005

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